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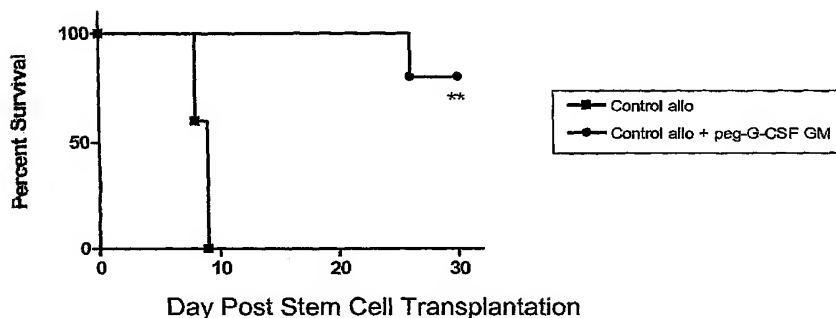
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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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see PCT Gazette No. 15/2005 of 14 April 2005, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: G-CSF DERIVATIVE FOR INDUCING IMMUNOLOGICAL TOLERANCE



(57) Abstract: The invention relates to a method, composition and use thereof for inducing immunological tolerance, in particular transplantation tolerance in a recipient and self-tolerance in a patient. Tolerance is preferably induced by administering a G-CSF derivative, or biologically active fragment, homolog or variant thereof, in particular peg-G-CSF, to a transplantation donor. Transplantation tolerance may reduce or prevent graft versus host disease or graft rejection and self-tolerance may prevent, treat or improve a condition in relation to an autoimmune disorder. The invention also relates to expanding and stimulating selected donor cells by administering a G-CSF derivative, preferably peg-G-CSF. The donor cells are preferably granulocyte-monocyte precursors cells and IL-10 secreting T cells.

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# INTERNATIONAL SEARCH REPORT

International application No.  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> Int. Cl. <sup>7</sup> : A61K 38/19, A61P 37/06, C07K 14/53, C12N 5/08 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WPIDS MEDLINE CA: polyethylene glycol, granulocyte colony stimulating factor, csf, gcsfhgcsf, neulasta, peg, graft versus host disease, gvhd, transplant, autotransplant, tolerance, donor, autoimmune, t cell, allogenic, interleukin 10, il10, stem cell		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Arpinati M <i>et al</i> , "Granulocyte-colony stimulating factor mobilizes T helper 2-inducing dendritic cells", <i>Blood</i> , 2000, 95(8):2484-2490 whole of document	1-5, 8-42, 45-51, 62-74, 77-79
Y	whole of document	6, 7, 43, 44, 75, 76
X	Pan L <i>et al</i> , "Pretreatment of Donor Mice With Granulocyte Colony-Stimulating Factor Polarizes Donor T Lymphocytes Toward Type-2 Cytokine Production and Reduces Severity of Experimental Graft-Versus-Host Disease", <i>Blood</i> , 1995, 86(12):4422-4429 whole of document	1-5, 8-25, 29-42, 46-51, 62-74, 77-79
Y	whole of document	6, 7, 43, 44, 75, 76
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family	
Date of the actual completion of the international search 19 November 2004		Date of mailing of the international search report - 9 FEB 2005
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929		Authorized officer  <b>GARETH COOK</b> Telephone No : (02) 6283 2541

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2004/001116

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Pan L <i>et al</i> , "Granulocyte Colony-Stimulating Factor-Mobilized Allogeneic Stem Cell Transplantation Maintains Graft-Versus-Leukemia Effects Through a Perforin-Dependent Pathway While Preventing Graft-Versus-Host Disease" <i>Blood</i> , 1999, 93(12):4071-4078 whole of document	1-5, 8-15, 26-37, 72-74, 77-79
Y	whole of document	6, 7, 43, 44, 75, 76
X	Willis F <i>et al</i> , "Pegfilgrastim", <i>Expert Opinion on Biological Therapy</i> , 2002, 2(8):985-992 whole of document	52-61
Y	whole of document	6, 7, 43, 44, 75, 76
X	Li EC, "Pegfilgrastim", <i>Journal of the Pharmacy Society of Wisconsin</i> , May/June 2003, 34-39 whole of document	52-61
Y	whole of document	6, 7, 43, 44, 75, 76
X	Yamasaki M <i>et al</i> , "Modification of Recombinant Human Granulocyte Colony Stimulating Factor (rhG-CSF) and Its Derivative ND28 with Polyethylene Glycol", <i>Journal of Biochemistry</i> , 1994, 115:814-819 whole of document	52-61
Y	whole of document	6, 7, 43, 44, 75, 76
P, X	Morris ES <i>et al</i> , "Donor treatment with pegylated G-CSF augments the generation of IL-10 producing regulatory T cells and promotes transplantation tolerance", <i>Blood</i> , 1 May 2004, , 103(9):3573-3581 whole of document	1-79
X	WO 2000/044785 A1 (Hoffman-La Roche Inc) 3 August 2000 whole of document	52-61, 69, 70, 72-79
X	Molineux G <i>et al</i> , "A new form of Filgrastim with sustained duration in vivo and enhanced ability to mobilize PBPC in both mice and humans", <i>Experimental Hematology</i> , 1999, 27:1724-1734 whole of document	52-61, 69, 70, 72-79
X	de Haan G <i>et al</i> , "Efficient mobilization of haematopoietic progenitors after a single injection of pegylated recombinant human granulocyte colony-stimulating factor in mouse strains with distinct marrow-cell pools", <i>British Journal of Haematology</i> , 2000, 110:638-646 whole of document	52-61, 69, 70, 72-79

## INTERNATIONAL SEARCH REPORT

International application No.

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### Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: **1-92 (partially)**  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
The claims in referring to a G-CSF-derivative, biologically active fragment, homolog or variant encompass any form of G-CSF. The specification only describes the derivative peg-G-CSF as having the properties desired, and there is no guidance in the description on other derivatives which have the desired properties. The claims have only been searched with respect to the derivative peg-G-CSF.
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

### Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2004/001116

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member	
WO 2000/044785	AT 246202	CZ 20012654	NZ 513113
	AU 26185/00	EP 1157037	SK 10352001
	BG 105851	EP 1369429	US 2003130193
	BR 0007781	HU 0203652	ZA 200105932
	CA 2361766	NO 20013700	
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.			
END OF ANNEX			